510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:
k041051

B. Purpose for Submission:
New device

C. Analyte:
Urea nitrogen

D. Type of Test:
Quantitative enzymatic assay

E. Applicant:
Hemagen Diagnostics Inc.

F. Proprietary and Established Names:
Raichem BUN Reagent (liquid)

G. Regulatory Information:

1. Regulation section:
   21 CFR §862.1770, Urea nitrogen test system
2. Classification:
   Class II
3. Product Code:
   CDQ
4. Panel:
   Chemistry (75)

H. Intended Use:

1. Intended use/Indication(s) for use:
   "This reagent is for the quantitative in vitro enzymatic determination of urea nitrogen in serum or plasma by measurement of the initial rate of reaction.

   This urea nitrogen test system is a device intended to measure urea nitrogen (an end-product of nitrogen metabolism) in serum or plasma. Measurements obtained by this device are used in the diagnosis and treatment of certain renal and metabolic diseases. The intended patient population may be adult, pediatric, and neonatal."

2. Special condition for use statement(s):
   This product is for prescription use only.

3. Special instrument Requirements:
   Roche COBAS Mira Chemistry System

I. Device Description:

This reagent is liquid, and is provided ready-to-use in vials. The reagent contains the following: -ketoglutarate, nicotinamide adenine dinucleotide (reduced), urease (Jack bean), glutamate dehydrogenase (microbial), buffers, stabilizers and fillers.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Roche COBAS Reagent for BUN
2. Predicate K number(s):
   k801116
3. Comparison with predicate:
   The two products have the same intended use, utilize the enzymatic reactions on the same instrument, have the same analytic range, use the matrices, and have the same stability.

K. Standard/Guidance Document Referenced (if applicable):

Area of Study	Reference Procedure	Procedure Title
Method Comparison/ Anticoagulant Studies	NCCLS EP9-A	User Comparison of Quantitative Clinical Laboratory Methods Using Patient Samples
Precision	NCCLS EP5-A	User Evaluation of Precision Performance of Clinical Chemistry Devices
Linearity	NCCLS EP6-A	Evaluation of the Linearity of Quantitative Methods
Interferences/ Cross-Reactivity	NCCLS EP7-A	Interference Testing in Clinical Chemistry
Guidance	FDA (Draft)	"Data for commercialization of original equipment manufacturer, secondary, and generic reagents for automated analyzers, 10 June 1996"

L. Test Principle:

This test is based on a series of enzymatic reactions that result in a measurable decrease in absorbance at 340 nm when NADH is oxidized to NAD. In the first step, hydrolysis of urea by urease to produces ammonia and carbon dioxide. In the second reaction, glutamate dehydrogenase catalyzes the reaction of α-ketoglutarate and ammonia. In this same reaction, two moles of reduced NAD (NADH) are oxidized to NAD for each mole of urea converted.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Serum studies were performed on serum according to the guidelines of NCCLS EP5-T. Serum in the normal range and in the abnormal (elevated) range was tested twice a day for 20 days in duplicate.

Precision of Raichem BUN Rate Reagent (n=20)

	Assay Values (mg/dL)			**Within Run**		**Total Imprecision**	
Level	Min	Max	**Mean**	Std Dev	% CV	Std Dev	% CV
Normal	13.8	16.1	14.7	0.4	2.4	0.5	3.4
Abnormal	44.2	52.8	48.1	0.9	1.9	1.5	3.2

b. Linearity/assay reportable range:

Studies performed according to NCCLS EP6-A. A urea-spiked sample was diluted to span the linear range. All ten dilutions and the zero level were read four times. Recovery was calculated from the assay mean; all recoveries were within the manufacturer's specification of 92.5% to 107.5% of the assigned value of the diluted sample. The data supports the claim of linearity to 80 mg/dL (114 mg/dL with auto-dilute feature on).

c. Traceability (controls, calibrators, or method):

No traceability was provided.

The sponsor reports the unopened shelf-life stability as 18 months at 2 to 8^{o} C. This was established by real-time testing under claimed storage conditions. On-board stability was determined by leaving an open reagent container on the instrument for 8 hours and tightly closed for 16 hours. In the uncooled reagent compartment there was less than 5% variance in the recovery of a low concentration BUN sample over five days, and less than 5% variance in the recovery of a high concentration BUN sample over four days (low reagent volume the fifth day). In the cooled reagent compartment, both the low and high concentration BUN samples had less than 10% variance over seven days, although the variance increased with time.

d. Detection limit:

Water was assayed twenty times in a single analytical run. The detection limit is calculated as the mean (or zero if the mean is less than zero) plus two standard deviations of the results. The observed mean and standard deviation was -0.31 and 0.46 mg/dL respectively. Therefore, the detection limit of the assay is 0.92 mg/dL BUN.

e. Analytical specificity:
Interference of hemoglobin, conjugated and unconjugated bilirubin, triglycerides, EDTA plasma, and heparinized plasma was evaluated according to NCCLS EP7-A. All substances showed <10% variance than the baseline and so were within the sponsor's specifications.

f. Assay cut-off:
Not applicable.

2. Comparison studies:
   a. Method comparison with predicate device:
   Values obtained from 101 serum samples ranging from 7.4 to 114 mg/dL and tested in duplicate on a Cobas MIRA analyzer using the predicate reagent and the Raichem reagent. Samples >80 mg/dL were automatically diluted and re-read. All regression statistics are within the manufacturer's specifications.

Comparison of Raichem BUN Reagent and Predicate

Value	Serum
Intercept	0.41
Slope	0.983
R^2 value	0.999
N	101
Range	7.4 to 114

   b. Matrix comparison:
   Not applicable.
3. Clinical studies:
   a. Clinical sensitivity:
   Not applicable.
   b. Clinical specificity:
   Not applicable.
   c. Other clinical supportive data (when a and b are not applicable):
   Not applicable.
4. Clinical cut-off:
   Not applicable.
5. Expected values/Reference range:
   Tietz reports a normal reference range of 7-18 mg/dL urea nitrogen (Fundamentals of Clinical Chemistry).

N. Conclusion:

The submitted information in this pre-market notification is complete and supports a substantial equivalence decision.